TITLE 410 INDIANA STATE DEPARTMENT OF HEALTH

LSA Document #15-39

SUMMARY/RESPONSE TO COMMENTS

The Indiana State Department of Health's (ISDH) Executive Board preliminarily adopted the Disease Reporting and Control Rule at 410 IAC 1-2.5 on March 11, 2015. ISDH published the proposed rule in the June 10, 2015, Indiana Register. A public hearing was held in Indianapolis on July 6, 2015, to solicit comments from the public on the proposed rule. No verbal or written comments were made during the public hearing.

The following parties made written comments after the public hearing, but during the public comment period:

Susan M. Kraska – Association for Professionals in Infection Control and Epidemiology
Mary Stepney – The Medical Foundation - South Bend

The ISDH laboratory sent out an online survey to their list of Indiana laboratories in order to receive comments on a particular disease listed in the new rule (Carbapenemase-producing carbapenem-resistant Enterobacteriaceae (CP-CRE)). The ISDH laboratory received forty-seven (47) hits to their online survey with twenty-seven (27) people completing the survey in its entirety.

The following parties responded to the online survey and wished to have their comments used in the public comment period:

Linda Rutherford – Reid Hospital
Rhonda Brune – Adams Memorial Hospital
Claudia Dant – Gibson General Hospital
Julie L. Oliver – Henry County Hospital
Julie H. Voirol – DeKalb Health Laboratory
Carol Yager – Fayette Regional
Audie Whitaker – Community Hospital Anderson
Donna Sexton – St. Vincent Dunn
Jaime Redkey – St. Vincent Hospital 86th Street
Cheryl R. Houin – St. Joseph Regional Medical Center
April Abbott – Deaconess Hospital
Pravin H. Patel, Ph.D. – Community Health Care System Munster
Mary Schoaff MT (ASCP) ICP – Lutheran Hospital Fort Wayne
Marijo Roiko – IU Health
Theresa Davison – Decatur County Memorial Hospital
Mary Stepney – The Medical Foundation South Bend
Angie Hughes – Community Hospital of Bremen
Claire Roembke – Franciscan St. Francis Health

Eric Surface – Woodlawn Hospital
John Sawatsky – IU Health Goshen Hospital
Leann Lawrence – Clark Memorial Hospital
Mary P. McDonald – Terre Haute Regional Hospital
Sherry Robbins – IU Health Goshen
Jerry Wheatley – Memorial Hospital and Health Care Center Jasper
Jean Knickerbocker – IUH La Porte Hospital
Vera Concho – Alverno Clinical Laboratory
Bonny Lewis Van – Marion County Public Health Department

The following party offered a written comment after the public comment period closed:

Angela M. Toth – Associate, The Corydon Group

The following is a summary of the comments received and ISDH's responses thereto (similar comments have been grouped together with one response):

Comment from Susan M. Kraska: The Indiana Chapter of the Association for Professionals in Infection Control and Epidemiology (APIC) appreciates the opportunity to provide input for the revision of the Communicable Disease Reporting Rule and the inclusion of 410 IAC 1-2.5-86 Carbapenemase-Producing Carbapenem-Resistant Enterobacteriaceae (CP-CRE) and the specific control measures recommended. APIC supports adoption of the recommended rule 410 IAC 1-2.5-86 and the inclusion of the proposed revision of the Communicable Disease Reporting Rule 410 IAC 1-2.5.

Response: Thank you for your comment. ISDH appreciates your continued support.

Comment from Mary Stepney: Not all laboratories use the same antimicrobial susceptibility categorization breakpoints so reporting will differ between facilities.

Response: The CP-CRE definition includes both zone diameter and minimum inhibitory concentration (MIC) criteria, thus eliminating the potential bias created by differing susceptibility breakpoints.

Comment from Mary Stepney: Infection Preventionists need to be aware of the mechanism of resistance to best advise in their facilities. How much working knowledge is required/expected of mechanism for the infection preventionist? Is this information required for nurses? How do we teach nurses this information?

Response: Infection Preventionists will be trained on CP-CRE's through the Indiana Association for Professionals in Infection Control and Epidemiology (APIC) and also from Indiana District trainings. This training will include a brief informational section on the mechanism of resistance. The bottom line is that a CP-CRE patient needs to be put into isolation regardless of the resistance mechanism.

Comment from Mary Stepney: Consistent acronym usage needed.

Response: At this time, we are limiting our reporting to members of the *Enterobacteriaceae*. The acronym that will be used to designate carbapenemase-producing carbapenem-resistant *Enterobacteriaceae* is CP-CRE. This may be expanded in the future; however, to include other non-*Enterobacteriaceae* carbapenem-resistant organisms. At such a time, the acronym to be used will be CP-CRO.

Comment from Mary Stepney: Clarify what isolates labs need to submit (issues outlined regarding Modified Hodge, CarbaNP, and susceptibility profile).

Response: Based on these comments, ISDH suggests the following modification to the rule:

> Isolates include organisms that are nonsusceptible to at least one (1) carbapenem antibiotic with MIC >=2 µg/ml or zone diameter <=22 mm (<=21 mm for ertapenem), and meet one (1) of the following criteria:
>
> (A) Positive for carbapenemase production by a phenotypic test (e.g., Modified Hodge or Carba NP).
>
> (B) Nonsusceptible to at least three (3) carbapenem antibiotics with MIC >=2 µg/ml or zone diameter <=22 mm (<=21 mm for ertapenem).
>
> (C) Positive for a carbapenemase gene marker.
>
> Only one (1) isolate that meets these criteria should be submitted if the same organism is repeatedly recovered from the same patient.

Comment from Julie H. Voirol: Respondents need clarification on whether the rule is referring to *Enterobacteriaceae* or all carbapenem-resistant organisms.

Response: At this time, ISDH is limiting our reporting to members of the *Enterobacteriaceae.* This may be expanded in the future; however, to include other non-*Enterobacteriaceae* carbapenem-resistant organisms.

Comment from Julie H. Voirol: Many laboratories currently do not perform phenotypic tests or do not have the ability/expertise to correctly identify carbapenemases.

Comment from Claudia Dant: More training is needed for testing.

Comment from Rhonda Brune; Claudia Dant; Carol Yager: There is a need for more resources, more expertise to help recognize MDROs.

Comment from Audie Whitaker: She would like a better definition and clarification of what a CRE is and how to test for it.

Comment from April Abbott: She would like education about CRE versus CPO versus MDRO versus CRO.

Comment from Julie L. Oliver: She would like updated information about CRE testing and screening.

Response: The ISDH Laboratories will be offering a CRE Workshop this fall, which will include both an instructional lecture, as well as hands-on workshop for use of both CarbaNP and Modified Hodge. We would highly encourage attendance at this event.

Comment from Mary Stepney; Angie Hughes: This may significantly reduce the number of isolate submissions.

Comment from Mary Stepney: This will reduce the number of organisms submitted, but have concerns about the false-positive and false-negative Modified Hodge tests.

Comment: There are some concerns with the sensitivity and specificity of the Modified Hodge Test and most laboratories do not use Carba NP test.

Response: We would encourage you to contact the ISDH Laboratories regarding any suspicious isolates that do not meet the CDR-submission criteria.

Comment from Julie H. Voirol; Carol Yager: Consider adding "resistance to third generation cephalosporins".

Response: This inclusion would add additional work for submitters. Our current criteria, which includes the assessment of phenotypic carbapenemase production, makes the assessment of cephalosporin resistance unnecessary.

Comment: Suggest an alternative for Modified Hodge test or Carba NP.

Response: PCR is another viable option for the assessment of carbapenemase markers. In addition, several research groups have published alternative testing methods to Modified Hodge or CarbaNP for the detection of carbapenemases; however, these tests are not FDA approved.

Comment from Cheryl R. Houin; Leann Lawrence: Some facilities would prefer five business days instead of three.

Response: If ISDH extends reporting from three business days to five business days, the facility's infection control response (i.e., initiation of contact precautions and laboratory testing) may be delayed.

Comment: There needs to be a standardization of terms because the questions refer to "carbapenem-resistant organisms" which implies organisms beyond Enterobacteriaceae (the definition should be more specific).

Response: For the purposes of the current rule revision, ISDH will use the term carbapenemase-producing carbapenem-resistant *Enterobacteriaceae* (CP-CRE). This may be modified in the future; however, to CP-CRO, to include other non-*Enterobacteriaceae* organisms.

Comment from Angie Hughes: She would define a "probable" and "suspected" CRE.

Response: As the mechanism of CP-CRE will be evaluated at the ISDH Laboratories, 'probable' or 'suspected' provides little additional information for the description of an isolate. The result will be 'present' or 'absent', and defined according to the type of carbapenemase.

Comment: Consider organisms that are non-susceptible to at least two carbapenem antibiotics since it a lot of work to send isolates.

Response: CP-CRE isolates that are resistant to a single carbapenem antibiotic are well-documented in the scientific literature. A retrospective analysis of isolates submitted to the ISDH Laboratories suggests that inclusion of isolates that are resistant to only two carbapenems, instead of at least one carbapenem, would only decrease isolate submission by ~2%. This retrospective review; however, does suggest that isolates resistant to at least three carbapenems, may not require a phenotypic assessment of carbapenemase production in order to be considered a putative CP-CRE.

Comment from Vera Concho: She stated that ISDH will need to define it so that ertapenem is not included in the verbage or ISDH will get more isolates.

Response: The inclusion of ertapenem came at the strong recommendations of Dr. Ken Thompson and the Centers for Disease Control and Prevention (CDC). Ertapenem is considered the most sensitive marker of CP-CRE, as CP-CRE that are susceptible to imipenem, meropenem, or doripenem have been well established in the scientific literature. The CDR requirement of an assessment of phenotypic carbapenemase production should limit the submission of inappropriate isolates.

Comment from Angie Hughes; Sherry Robbins: Many laboratories have limited resources and staffing so they may have trouble testing isolates.

Comment from Claudia Dant; Julie L. Oliver: It would not be cost effective to perform PCR or CarbaNP testing in-house.

Response: The cost of testing may be defrayed by considering 1) the cost of shipping isolates to the ISDH (category B), as well as 2) the costs associated with patient isolation. If a phenotypic assessment of carbapenemase production is not performed, more isolates will need to be sent to the ISDH Laboratories for confirmatory testing. A retrospective review of isolates submitted to the ISDH Laboratories suggests that as many as one-third of these isolates would not have been submitted if a phenotypic assessment of carbapenemase production had been conducted prior to submission. In our institution, the cost of a CarbaNP test is $2-$3, whereas shipping of an isolate is $15-$25, depending on the point of origin.

Comment from Rhonda Brune; Julie L. Oliver; Theresa Davison; Leann Lawrence; Sherry Robbins : Many facilities send isolates to a reference lab or state lab for confirmatory testing.

Response: Isolates submitted to a reference laboratory must be submitted according to the rule.

Comment from Cheryl R. Houin; Jerry Wheatley: More rapid notification and confirmatory test results.

Response: The ISDH Laboratories are currently working on our diagnostic algorithm as well as testing capacity to minimize the turn-around time associated with isolate submission.

Comment from Claire Roembke: She would like to have additional information on finding patients' previous history of healthcare exposure.

Response: When CP-CRE patients are transferred between facilities, the sending facility should send an inter-facility transfer form along with any laboratory reports to the receiving facility. This will help the receiving facility determine a patient's history of healthcare exposure. The ISDH Antibiotic Resistance (AR) Advisory Committee has created an AR subgroup of the committee that will work on developing a state inter-facility transfer form that can be used by various facilities.

Comment from Linda Rutherford: She would like information about the cost and process of sending the isolates to ISDH. It is difficult to reach anyone to provide an assigned number prior to sending the isolate.

Response: There is no cost for isolate submission to the ISDH Laboratories. Isolates will be submitted through LimsNet, which will remove the requirement of a pre-assigned number. To establish a LimsNet account, please contact the help desk at (888) 535-0011 or email LimsAppSupport@isdh.in.gov. Isolates should be shipped Category B.

Comment from Julie H. Voirol: She hopes that the State is willing to staff ISDH with enough trained laboratory staff to handle the large influx of work in a timely manner.

Response: ISDH is endeavoring to streamline our algorithm to improve our testing capacity and turn-around time. ISDH, like many of you, would benefit from additional staffing.

Comment from Mary Schoaff: She would like a little more clarity in the definition.

Comment: Suggest an alternative for Modified Hodge test or Carba NP.

Comment: Consider organisms that are non-susceptible to at least two carbapenem antibiotics since it a lot of work to send isolates.

Comment from April Abbott: I recommend inclusion of molecular methods.

Comment from April Abbott: An isolate with an ertapenem zone diameter of 22mm is susceptible.

Comment from Claudia Dant*:* Suggest alternative for Modified Hodge test or send isolate without confirmation by phenotypic method.

Response: Based on these comments, ISDH suggests the following modification to the rule:

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> (C) Positive for a carbapenemase gene marker.
>
> Only one (1) isolate that meets these criteria should be submitted if the same organism is repeatedly recovered from the same patient.

Comment from Angela M. Toth: It has come to our attention that the Indiana Code and the Indiana Administrative Code are inconsistent regarding the required reporting of HIV cases. The language of 410 IAC 1-2.5-75 requires reporting of HIV cases to the local health officer while IC 16-41-2-3 requires reporting to the state department of health. It is our opinion that the rules should be consistent and transparent.

Response: Thank you for your comment. ISDH has remedied this issue by making modifications to the rule language of 410 IAC 1-2.5-75(b) and (d) to be consistent with IC 16-41-2-3.